

***Remarks***

Reconsideration of this Application is respectfully requested. Claims 3 and 47-50 are pending in the application, with claims 3 and 47-50 being the independent claims. Claims 3 and 47-50 are pending and under consideration. Under 37 C.F.R. § 1.116(b), claims 47-50 have been amended to place them in better form for allowance or appeal. Support for these amendments may be found, *inter alia*, in the specification as-filed at paragraphs [0003], [0005], [0009], [0017], [0022-0025], [0028], [0032], [0033], [0036], [0037], [0042], [0049], [0060-0064], [0068], [0069], Examples 1-7 [0073-0087], Examples 8-11 [0090-0102] and Table 1. These changes are believed to introduce no new matter, and their entry is respectfully requested. Claims 51-70 have been withdrawn by the Examiner as allegedly being directed to a non-elected invention.

Based on the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

***Election/Restriction***

The Examiner has withdrawn newly-presented claims 51-70 as allegedly being directed to a distinct invention from the compositions recited in claims 3 and 47-50. (Office Action of 10/26/2006, hereinafter "OA", at page 2.) The Examiner asserts that "[s]ince applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation of prosecution on the merits," citing MPEP § 821.03. (*See Id.*) Applicants respectfully traverse the withdrawal of claims 51-70.

**A. Claims 54, 58, 62, 66 and 70**

Applicants respectfully assert that claims 54, 58, 62, 66 and 70 should be rejoined with the claims under consideration in the present application because they depend from either allowable claim 3 or claims 47-50, which are also believed by Applicants to be in condition for allowance. (*See* pages 12-19, *infra*). Presently-withdrawn claims 54, 58, 62, 66 and 70 are directed to a method for producing a polypeptide using the nucleic acid sequences recited in claims 3 and 47-50 (*i.e.*, the nucleic acid sequence of SEQ ID NO: 115 and sequences having 95%, 90%, 85% or 83% identity with SEQ ID NO:115). The USPTO published a Notice in the March 26, 1996 Official Gazette setting forth the guidelines for the treatment of product and process claims in light of the Federal Circuit's decisions in *In re Ochiai*, 71 F.3d 1565 (Fed. Cir. 1995), and *In re Brouwer*, 77 F.3d 422 (Fed. Cir. 1996). *See* 1184 OG 86 (March 26, 1996). Specifically, the Notice states that in the case of an elected product claim, rejoinder will be permitted when a product claim is found allowable and the withdrawn process claim depends from or otherwise includes all the limitations of an allowed product claim. *See Id.*

In the present case, the Examiner has essentially restricted between the product recited in claims 3 and 47-50, and methods of using the product, as recited in claims 54, 58, 62, 66 and 70. In the Office Action dated October 24, 2006, the Examiner stated that claim 3 is allowable because "the prior art does not describe an isolated nucleic acid comprising SEQ ID NO:115." (OA at page 4). Although the Examiner has rejected claims 47-50 under 35 U.S.C. §112, first paragraph, Applicants believe this rejection will be overcome, and that presently-pending claims 47-50 are in condition for allowance. (*See* pages 12-19, *infra*). Thus, in view of the guidelines set forth in the March 26, 1996

Official Gazette Notice, as well as the Federal Circuit's decisions in *In re Ochiai* and *In re Brouwer*, Applicants respectfully request reconsideration and rejoinder of withdrawn method claims 54, 58, 62, 66 and 70 with presently-pending product claims 3 and 47-50.

**B. Claims 51-53, 55-57, 59-61, 63-65 and 67-69**

The Examiner has also withdrawn claims 51-53, 55-57, 59-61, 63-65 and 67-69 from consideration, asserting that they are directed to distinct compositions "such as a genetically engineered host cell, comprising a recombinant vector comprising a distinct polynucleotide sequence." (OA at page 2.) Applicants respectfully traverse this restriction.

**(i) Claims 51-53**

Claims 51-53 should be rejoined and fully examined for patentability in accordance with 37 CFR §1.104 because they were presented for examination prior to final rejection or allowance, and require all the limitations of allowable claim 3. *See* MPEP §821.04(a). Claims 51-53 depend directly or indirectly from claim 3, and are directed to compositions requiring the allowable product of claim 3 (SEQ ID NO: 115). In the Office Action of October 24, 2006, the Examiner essentially restricted claims 51-53 from the present application by withdrawing them as allegedly being directed to a non-elected invention. (OA at page 2). Applicants respectfully traverse this restriction.

Section 821.04(a) of the MPEP states that an amendment presenting additional claims that depend from, or otherwise require all the limitations of, an allowable claim *will be entered as a matter of right* if the amendment is presented prior to final rejection or allowance, whichever is earlier. *See* MPEP 821.04(a). In this case, the additional claims presented in the September 13, 2006 Amendment and Reply (including claims 51-

53) were submitted before a final rejection was issued. Additionally, the Examiner has indicated that claim 3, directed to the nucleic acid sequence of SEQ ID NO:115, is allowable. (*See* OA, page 4). Claims 51-53 depend directly or indirectly from claim 3, and recite compositions requiring the allowable product of claim 3 (SEQ ID NO: 115). Furthermore, claim 3 is a generic linking claim with regard to claims 51-53. *See* MPEP §809. When all claims directed to the elected invention are allowable, should any linking claim be allowable, the restriction requirement between the linked inventions must be withdrawn. *See* MPEP §809. Any claims directed to the nonelected invention(s), previously withdrawn from consideration, and which depend from or require all the limitations of the allowable linking claim must be rejoined and will be fully examined for patentability. *See* MPEP §809. Thus, according to MPEP §§ 809 and 821.04(a), at least claims 51-53, all of which depend directly or indirectly from allowable claim 3 should have been considered in the Office Action of October 24, 2006. Accordingly, Applicants respectfully assert that claims 51-53 should be rejoined with the presently-pending claims and fully examined for patentability in accordance with 37 CFR §1.104.

**(ii) Claims 55-57, 59-61, 63-65 and 67-69**

Claims 55-57, 59-61, 63-65 and 67-69 should be rejoined and fully examined for patentability in accordance with 37 CFR §1.104 because they depend directly or indirectly from claims 47-50, and although the Examiner has rejected independent claims 47-50 under 35 U.S.C. §112, first paragraph, this rejection is believed to have been overcome, putting claims 47-50 in condition for allowance. *See* MPEP §821.04(a). Claims 55-57, 59-61, 63-65 and 67-69 are directed to compositions such as recombinant

vectors and genetically engineered host cells, requiring either the allowable product of claim 3 (SEQ ID NO: 115), or sequences that have 95%, 90%, 85% or 83% identity with SEQ ID NO: 115. In the Office Action of October 24, 2006, the Examiner essentially restricted claims 55-57, 59-61, 63-65 and 67-69 from the present application by withdrawing them as being allegedly directed to a non-elected invention. (OA at page 2). Applicants respectfully traverse this restriction.

Section 821.04(a) of the MPEP states that when restriction has been required between independent or distinct products, or between independent or distinct processes, and all claims directed to an elected invention are allowable, any restriction requirement between the elected invention and any nonelected invention that depends from or otherwise requires all the limitations of an allowable claim should be withdrawn. *See* MPEP §821.04(a). In this case, although genetically engineered host cells and recombinant vector could technically be classified into a different class and subclass, the search for SEQ ID NO:115 or sequences having 95%, 90%, 85% or 83% identity with SEQ ID NO: 115 would be coextensive with the different classes comprising host cells and recombinant vectors. As noted above, the Examiner stated in the Office Action of October 24, 2006, that SEQ ID NO: 115 is found to be free of the prior art. (OA, page 4). Thus, any composition that includes SEQ ID NO: 115 and is not a product of nature will also be free of the prior art. Furthermore, Applicants assert that examination of claims 55-57, 59-61, 63-65 and 67-69 would not impose a burden on the examiner because the examiner has not established that the search for SEQ ID NO:115 would not have provided results pertinent to these claims. *See* MPEP §808.02. Accordingly, since claims 55-57, 59-61, 63-65 and 67-69 are directed to compositions encompassing an

allowable product, Applicants respectfully request that they be rejoined and fully examined for patentability in accordance with 37 CFR §1.104.

***Rejections under 35 U.S.C. § 112, first paragraph***

**A. Claims 47-50 do not contain new matter**

The Examiner has rejected claims 47-50 under 35 U.S.C. § 112, first paragraph, asserting that the amendments of September 13, 2006, introduce new matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art to that the inventor had possession of the inventions as now claimed. (OA at page 3.) Applicants respectfully traverse this rejection.

The specification and claims, as originally filed, provide proper descriptive support for the amendments of September 13, 2006, including the subject matter of claims 47-50. Presently-pending claims 47-50 are directed to an isolated polynucleotide comprising a nucleic acid sequence from 83-100% identical to the sequence of SEQ ID NO: 115, wherein the isolated polynucleotide encodes a toxin capable of binding to a sodium channel.

Written description does not require that the subject matter of the claim need be described literally, *i.e.*, using the same terms or *in haec verba*, in order for the disclosure to satisfy the description requirement. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. *See, e.g., Vas-Cath, Inc. v Mahurkar*, 935 F.2d 1555 at 1563 (Fed. Cir. 1991); *Martin v. Johnson*, 454 F.2d 746, 751 (CCPA 1972) (stating "the

description need not be in *ipsis verbis* [i.e., "in the same words"] to be sufficient"); *see also* MPEP §2163.

Additionally, the "Methodology for Determining Adequacy of Written Description" found at section 2163.II.A.2. of the MPEP provides that, prior to determining whether the disclosure satisfies the written description requirement for the claimed subject matter, an Examiner should review the claims and the *entire specification, including the specific embodiments, figures, and sequence listings*, to understand how the Applicant provides support for the various features of the claimed invention.

In this case, a skilled artisan would have understood the inventor to be in possession of the claimed invention based on the disclosure in the specification and sequence listing as originally filed, which provide descriptive support for the nucleic acid sequences that are at least 95%, 90%, 85% and 83% identical to SEQ ID NO:115. For example, Table 1, column D, on page 3 of the specification discloses a list of 71 nucleic acid sequences<sup>1</sup> that encode isolated scorpion toxins. (specification at page 3). Table 1 and the sequence listing are part of the specification, and should be considered when evaluating the adequacy of the written description.

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<sup>1</sup> These sequences also appear in the sequence listing as originally filed.

<u>Species</u>	<u>SEQ ID</u> <u>nucleic acid</u> <u>coding region of</u> <u>mature toxin</u>	<u>% identity with</u> <u>SEQ ID 115</u>	<u>SEQ ID</u> <u>primary protein</u> <u>structure of mature</u> <u>toxin</u>	<u>% identity with</u> <u>SEQ ID 116</u>
<i>C. exilicauda</i>	43	86.5 %	44	75%
<i>C. exilicauda</i>	47	87 %	48	76.5%
<i>C. nocius</i>	91	87.7%	92	74.2%
<i>C. elegans</i>	111	82.8%	112	73.3%
<i>C. elegans</i>	<b>115</b>	<b>100%</b>	<b>116</b>	<b>100%</b>
<i>C. elegans</i>	119	99.5%	120	95.3%
<i>C. sculpturatus</i>	151	88.5%	152	79.6%
<i>C. sculpturatus</i>	195	88%	196	76.5%

The sequences in the above table are those sequences that share the closest homology with SEQ ID NO:115 as determined by Examiner Desai's sequence search. (See APPENDIX A, attached hereto). The percent homology that each molecule listed in Table 1 has with SEQ ID NO:115 is an inherent feature of each sequence described in the specification. The percent homology between the sequences is a fact based on the structure of the sequences disclosed in the specification and sequence listing. The determination of percent identity between nucleic acid sequences was within the skill of the ordinary artisan as of the filing date of this application.

The sequences listed in the above table are part of the specification as-filed. As shown in the above table, SEQ ID NOs: 43, 47, 91, 111, 119, 151, and 195 share 86.5%, 87%, 87.7%, 82.8%, 99.5%, 88.5%, and 88% sequence identity with SEQ ID NO:115, respectively. Applicants assert that the specification as-filed, including the sequence listing, would have reasonably conveyed to one skilled in the relevant art that the inventors had possession of the claimed nucleic acid sequences having 95%, 90%, 85% or 83% identity with SEQ ID NO:115 at the time the application was filed. Therefore,



the specification provides adequate written description under 35 U.S.C. § 112, first paragraph, for a range of sequences which possess from 83% to 100% sequence similarity with SEQ ID NO:115, as recited in claims 47-50. Accordingly, this rejection is believed to have been overcome. Reconsideration and withdrawal of the New Matter rejection of claims 47-50 is respectfully requested.

**B. The specification provides proper written descriptive support for claims 47-50**

The Examiner has rejected claims 47-50 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. More specifically, the Examiner asserts that the recited subject matter was not described in "the specification in such a way as to convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." (OA at pages 3-4). The Examiner also asserts that "[o]ne of skill in the art cannot visualize or recognize which nucleic acid sequences can be modified and/or mutated such that the polynucleotide with reduced percent identity retains the function of a toxin affecting sodium and potassium channel activity as disclosed for SEQ ID NO:115." (OA at pages 3-4). Applicants respectfully traverse this rejection.

The specification as-filed provides adequate written descriptive support for the nucleic acids recited in claims 47-50, because a person of ordinary skill at the time of filing could have visualized or recognized the identity of the members of the recited genus based on recited functional requirements and known structural similarities shared by polynucleotides that are at least 95%, 90%, 85% and 83% identical to SEQ ID NO:115. More specifically, the ordinary artisan reading the specification in conjunction

with what was generally known in the art of scorpion toxins would have known that the sequences that are at least 95%, 90%, 85% or 83% identical to SEQ ID NO:115 would need to bind to the Na<sup>+</sup> channel and possess four cysteine bonds to fall within the scope of claims 47-50.

An objective standard for determining compliance with the written description requirement of 35 U.S.C. §112, first paragraph, is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed?" *In re Gosteli*, 872 F.2d 1008, 1012 (Fed. Cir. 1989), *see also* MPEP 2163.02. An applicant may show possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *See Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997). Moreover, the disclosure of a species has also been found to be sufficient to support a claimed genus when the disclosure of species would lead a person of ordinary skill to the genus. *See In re Herschler*, 591 F.2d 693 (CCPA 1979); *see also* MPEP 2163.05. ). In *Herschler*, the Court held that the disclosure of one corticosteroid was sufficient to support "physiologically active steroid" because the use would lead one of ordinary skill to the entire class of compounds. 591 F.2d at 697. The Federal Circuit has held that when generic elements of a claim are so well known and thoroughly characterized in the art that their recitation alone is sufficient to convey distinguishing information regarding their identity, the written description requirement for those elements is fully satisfied. *See Amgen Inc. v. Hoechst Marion Roussel Inc.*, 65 U.S.P.Q.2d 1385, 1398 (Fed. Cir. 2003). Another important consideration in assessing written description of a claimed

invention is the knowledge of one skilled in the art. *See Bilstad v. Wakalopulos*, 386 F.3d 1116, 1126 (Fed. Cir. 2004).

**(i) The encoded toxins of claims 47-50 must be capable of binding to Na<sup>+</sup> channels**

In this case, claims 47-50 have been amended to recite an isolated polynucleotide comprising a nucleic acid sequence from 83-100% identical to the sequence of SEQ ID NO: 115, wherein the isolated polynucleotide encodes a toxin capable of binding to a sodium channel. As discussed above, the specification as-filed, including the sequence listing, provides proper written descriptive support under 35 U.S.C. §112, first paragraph, for polynucleotides that are at least 95%, 90%, 85% and 83% identical to SEQ ID NO:115, as recited in claims 47-50. Furthermore, all of the publications cited in the specification have been incorporated by reference in their entirety, and thereby provide additional descriptive support for the presently pending claims. (specification paragraph [0105]).

Applicants explain in the specification that scorpion toxins generally fall into two categories: the long chain toxins, 60-76 amino acids in length, which block the Na<sup>+</sup> channel in excitable cells; and the short chain toxins, 29-41 amino acids in length that affect K<sup>+</sup> channels. (specification paragraph [0004]). The claimed toxins are all Na<sup>+</sup> channel toxins, 60-76 amino acids in length, and they all bind to the membrane bound sodium channel. (specification paragraph [0005]). It is the binding of the toxin to the cation channel (the Na<sup>+</sup> channel) that causes most of the toxicological symptoms in a patient. (specification paragraph [0009]; *see also*, Dehesa-Davilla, page 225).

The specification describes isolated and purified scorpion toxin nucleic acid sequences in the sequence listing, as well as in Table 1. The ordinary artisan reading the specification in light of what was known in the art would have recognized that the claimed sequences fall into the genus of long chain Na<sup>+</sup> channel blocking toxins. (*See* specification paragraph [0004]). Thus, the ordinary artisan as of the filing date would have understood that claims drawn to SEQ ID NO:115 or sequences having 95%, 90%, 85% and 83% sequence identity with SEQ ID NO: 115 are directed to Na<sup>+</sup> channel blocking toxins.

**(ii) The encoded toxins of claims 47-50 possess a common structural motif**

The Na<sup>+</sup> channel toxins from scorpions also possess a common structural motif. Applicants explain in the specification that these Na<sup>+</sup> channel affecting scorpion toxins possess eight cysteine residues which form four cysteine bonds in the mature toxin. (specification paragraph [0004]; *see also Possani et al.* at page 290, column 2). The common structural motif consists of one stretch of  $\alpha$  helix plus three strands of  $\beta$  sheet in antiparallel arrangement, connected by variable regions forming loops. (specification paragraph [0004]; *see also Possani et al.* p 287, 290). The cysteine residues are numbered consecutively 1-8 from the N- to the C- terminal of the toxin. Cysteine residues 1 and 8, 2 and 5, 3 and 6, as well as residues 4 and 7 form the four disulfide bridges. These disulfide bonds are conserved in all of the Na<sup>+</sup> channel blocking scorpion toxins that were known as of the filing date of the presently-pending application, including the sequences disclosed in the specification. (specification paragraph [0004]; *see also Possani et al.* p 290, column 2; *see also APPENDIX B* attached hereto, which

shows a sequence alignment of the sodium channel toxins disclosed in the specification, and highlights the conserved cysteine residues). In fact, as of the filing date of the present application, all Na<sup>+</sup> channel-specific toxins were known to be stabilized by four disulfide bridges. (specification paragraph [0004]; *see also* Possani *et al.* p 287). Thus, the ordinary artisan reading the specification in light of what was known in the art would have recognized and understood that the recited sequences having 95%, 90%, 85% and 83% sequence identity with SEQ ID NO: 115 would also possess the conserved structural motif of four cysteine bonds.

Based on the combination of what was known in the art about scorpion toxins at the time of filing and the disclosure of seven species of nucleic acid that fall within the scope of claims 47-50, the specification conveys to one of ordinary skill in the art that the recited polynucleotides fall into the genus of long chain Na<sup>+</sup> channel-blocking toxins possessing a conserved structural motif of four cysteine bonds.

**(iii) The USPTO's Written Description Guidelines  
Support a Finding of Proper Written Descriptive Support for  
Claims 47-50**

The USPTO's "*Revised Interim Written Description Guidelines Training Materials*" (hereinafter, "*Guidelines*") provides 18 examples describing how to determine whether the written description requirement of 35 U.S.C. §112, paragraph 1, is satisfied. The facts set forth in Example 14 are almost identical to the present situation, and support a finding of proper written descriptive support for presently-pending claims 47-50.

First, the language of claims 47-50 is extremely similar in form and substance to that of the sample claim provided in Example 14, which recites:

A protein having SEQ ID NO: 3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of  $A \rightarrow B$ .

*Guidelines*, p. 53. Similarly, claims 47-50 require that the claimed polynucleotide is at least 83% identical to SEQ ID NO:115 (the reference compound) and encodes a toxin that is capable of binding to a sodium channel, which is an essential feature of the claimed invention. Thus, the first requirement of Example 14 is met.

Second, the *Guidelines* state that a search of the prior art indicated that exemplified SEQ ID NO: 3 was novel and unobvious. *Id.* at page 54. In the present case, the Examiner stated in the Office Action of October 24, 2006, that the prior art does not describe an isolated nucleic acid comprising SEQ ID NO: 115, which is recited in claims 47-50. (OA at page 4). Thus, the second requirement set forth in Example 14 has been satisfied with regard to currently pending claims 47-50.

Third, an actual reduction to practice of a single disclosed species was deemed sufficient to support the recited genus of proteins that must be variants of exemplified SEQ ID NO: 3. *See Guidelines*, p. 54. The *Guidelines* state that the actual reduction to practice one species was sufficient because all of the variants were required to possess the specific functional activity and had a high percent structural identity with the reference compound. *See Guidelines*, p. 54. In the present case, Applicants have shown possession of the claimed invention by a reduction to practice as evidenced by the descriptive support for at least seven sequences that fall within the scope of the claims, as well as support for the functional element of the claims. (*See* specification, Table 1,

and the sequence listing). Thus, the third requirement set forth in Example 14 of the *Guidelines* has been satisfied.

Fourth, procedures for making variants of exemplified SEQ ID NO:3 which have 95% identity to SEQ ID NO:3 and retain its activity were conventional in the art. *See Guidelines*, p. 53. In the present case, methods for making variants that are at least 83% identical to the reference compound were known in the art at the time of filing, and are described in our specification. (*See Molecular Cloning: A Laboratory Manual* (2<sup>nd</sup> ed.), Sambrook *et al.* (Cold Spring Harbor Lab. Press, 1989), chapters 15-18; *see also* specification [0040] ). Thus, the fourth requirement set forth in Example 14 of the *Guidelines* has been satisfied with regard to presently pending claims 47-50.

Fifth, an assay was described in the specification that identified the other proteins having the binding activity recited in the example claim. *See Guidelines*, p. 53. In the present case, the toxins that are at least 95%, 90%, 85% or 83% identical to SEQ ID NO:115 can easily be tested for their binding to the Na<sup>+</sup> channel. (specification paragraph [0005]; *see also* Couraud *et al.* p10-12.) Although there are many different ways to test the binding of a toxin to a Na<sup>+</sup> channel, one test described in the specification through an incorporated reference uses a rat synaptosome and a labeled toxin. (specification paragraph [0005]; *see also* Couraud *et al.* p10-12). Thus, the fifth requirement set forth in Example 14 of the *Guidelines* has been satisfied with regard to presently pending claims 47-50.

Based on the requirements set forth in Example 14 of the USPTO's *Revised Interim Written Description Guidelines Training Materials*, as well as the common structural motifs and functional requirements, the specification conveys to a person of

ordinary skill in the art that the inventors had possession of, and broadly described, an isolated polynucleotide comprising a nucleic acid sequence from 83-100% identical to SEQ ID NO:155, wherein the isolated polynucleotide encodes a toxin that is capable of binding to a sodium channel. Thus, the specification provides adequate written description under 35 U.S.C. §112, first paragraph, for an isolated polynucleotide as recited in presently-amended independent claims 47-50, as well as those claims which depend therefrom. Accordingly, this rejection is believed to have been overcome. Reconsideration and withdrawal of the rejection of claims 47-50 is respectfully requested.

### ***Conclusion***

The Examiner has indicated that claim 3 directed to SEQ ID NO: 115 is allowable.

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.



January 24, 2007  
Amendment and Reply to Office Action of October 24, 2006

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CORONA VILLEGAS *et al.*  
Appl. No. 10/721,793

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

A handwritten signature in black ink, reading "Laura Vogel". The signature is fluid and cursive, with the first name "Laura" and last name "Vogel" clearly distinguishable.

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Date: January 24, 2007

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Scoring table: IDENTITY NUC  
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Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	192	100.0	192	9	US-10-721-793-115
2	192	100.0	323	9	US-10-721-793-113
3	190.4	99.2	192	9	US-10-721-793-119
4	190.4	99.2	323	9	US-10-721-793-117
5	156.8	81.7	192	9	US-10-721-793-151
6	156.8	81.7	320	9	US-10-721-793-149
7	155.2	80.8	192	9	US-10-721-793-195
8	155.2	80.8	320	9	US-10-721-793-193
9	152	79.2	192	9	US-10-721-793-47
10	152	79.2	258	9	US-10-721-793-45
11	150.4	78.3	192	9	US-10-721-793-43
12	150.4	78.3	254	9	US-10-721-793-41
13	145.4	75.7	198	9	US-10-721-793-91
14	145.4	75.7	323	9	US-10-721-793-89
15	126.8	66.0	189	9	US-10-721-793-111
16	126.8	66.0	311	9	US-10-721-793-109
17	124.6	64.9	323	9	US-10-721-793-101
18	124.6	64.9	323	9	US-10-721-793-105
19	123.2	64.2	192	9	US-10-721-793-103
20	123.2	64.2	192	9	US-10-721-793-107
21	123	64.1	198	9	US-10-721-793-147
22	123	64.1	198	9	US-10-721-793-175
23	123	64.1	323	9	US-10-721-793-145

24	123	64.1	323	9	US-10-721-793-173	Sequence 173, App
25	119.8	62.4	198	9	US-10-721-793-67	Sequence 67, Appl
26	119.8	62.4	198	9	US-10-721-793-71	Sequence 71, Appl
27	119.8	62.4	198	9	US-10-721-793-159	Sequence 159, App
28	119.8	62.4	198	9	US-10-721-793-163	Sequence 163, App
29	119.8	62.4	322	9	US-10-721-793-65	Sequence 65, Appl
30	119.8	62.4	322	9	US-10-721-793-69	Sequence 69, App
31	119.8	62.4	323	9	US-10-721-793-157	Sequence 157, App
32	119.8	62.4	323	9	US-10-721-793-161	Sequence 161, App
33	118.2	61.6	198	9	US-10-721-793-139	Sequence 139, App
34	118.2	61.6	198	9	US-10-721-793-155	Sequence 155, App
35	118.2	61.6	323	9	US-10-721-793-137	Sequence 137, App
36	118.2	61.6	323	9	US-10-721-793-83	Sequence 83, Appl
37	116.6	60.7	195	9	US-10-721-793-81	Sequence 81, Appl
38	116.6	60.7	274	9	US-10-721-793-97	Sequence 97, Appl
39	116.6	60.7	323	9	US-10-721-793-167	Sequence 167, App
40	115	59.9	195	9	US-10-721-793-171	Sequence 171, App
41	115	59.9	195	9	US-10-721-793-165	Sequence 165, App
42	115	59.9	323	9	US-10-721-793-169	Sequence 169, App
43	115	59.9	323	9	US-10-721-793-23	Sequence 23, Appl
44	113.4	59.1	195	9	US-10-721-793-143	Sequence 143, App
45	113.4	59.1	195	9	US-10-721-793-143	Sequence 143, App

ALIGNMENTS

RESULT 1  
US-10-721-793-115  
; Sequence 115, Application US/10721793  
; Publication No. US2005005311A1  
; GENERAL INFORMATION:  
; APPLICANT: Corona Villegas, Miguel  
; APPLICANT: Valdez Cruz, Norma Adriana  
; APPLICANT: Gurrola Briones, Georgina  
; APPLICANT: Becerril Lujan, Baltazar  
; APPLICANT: Possani Postay, Lourival Domingos  
; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the  
; TITLE OF INVENTION: Venom of Scorpions of the Genus Centruroides  
; FILE REFERENCE: 2099.0070001  
; CURRENT APPLICATION NUMBER: US/10/721,793  
; CURRENT FILING DATE: 2003-11-26  
; PRIOR APPLICATION NUMBER: US 60/430,067  
; PRIOR FILING DATE: 2002-12-02  
; NUMBER OF SEQ ID NOS: 294  
; SOFTWARE: PatentIn version 3.1  
; SEQ ID NO 115  
; LENGTH: 192  
; TYPE: DNA  
; ORGANISM: Centruroides elegans  
; FEATURE:  
; NAME/KEY: CDS  
; LOCATION: (1)..(192)  
; OTHER INFORMATION: Product= Sodium-channel modifier toxin  
US-10-721-793-115

Query Match 100.0%; Score 192; DB 9; Length 192;  
Best Local Similarity 100.0%; Pred. No. 1.1e-53;  
Matches 192; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy	1	AAGACGGTTATCTGCTGACAGCGCGCTGCACATACACTTGTGGATATTGGAGAA	60
Db	1	AAGACGGTTATCTGCTGACAGCGCGCTGCACATACACTTGTGGATATTGGAGAA	60
Qy	61	AACAAATCTGCAATAGGGAATGCACATGGGAAGCAGAGAGGTAATTACGGCTATTGC	120
Db	61	AACAAATCTGCAATAGGGAATGCACATGGGAAGCAGAGAGGTAATTACGGCTATTGC	120
Qy	121	TACGGATTGGGCTATTGGCAAGGATTGTCCGATAGTACCGACTTTGGCCCCCTTCT	180
Db	121	TACGGATTGGGCTATTGGCAAGGATTGTCCGATAGTACCGACTTTGGCCCCCTTCT	180

QY 181 AATAAAGATGC 192  
 DB 181 AATAAAGATGC 192

## RESULT 2

US-10-721-793-113  
 ; Sequence 113, Application US/10721793  
 ; Publication No. US20050065331A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Corona Villegas, Miguel  
 ; APPLICANT: Garcia Rodriguez, Ma Consuelo  
 ; APPLICANT: Valdez Cruz, Norma Adriana  
 ; APPLICANT: Gurrola Briones, Georgina  
 ; APPLICANT: Becerril Lujan, Baltazar  
 ; APPLICANT: Possani Postay, Lourival Domingos  
 ; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the  
 ; FILE REFERENCE: 2099.0070001  
 ; CURRENT APPLICATION NUMBER: US/10/721,793  
 ; CURRENT FILING DATE: 2003-11-26  
 ; PRIOR APPLICATION NUMBER: US 60/430,067  
 ; PRIOR FILING DATE: 2002-12-02  
 ; NUMBER OF SEQ ID NOS: 294  
 ; SOFTWARE: Patent in version 3.1  
 ; SEQ ID NO 113  
 ; LENGTH: 323  
 ; TYPE: DNA  
 ; ORGANISM: Centruroides elegans  
 ; FEATURE:  
 ; NAME/KEY: CDS  
 ; LOCATION: (5)..(265)  
 ; OTHER INFORMATION: Product= Sodium-channel modifier toxin precursor  
 ; OTHER INFORMATION: In the mature peptide, the last Cys is amidated, and the last Gly  
 ; OTHER INFORMATION: and the last 2 basic aminoacids are cut  
 ; FEATURE:  
 ; NAME/KEY: 3'UTR  
 ; LOCATION: (269)..(323)  
 ; OTHER INFORMATION:  
 ; FEATURE:  
 ; NAME/KEY: 5'UTR  
 ; LOCATION: (1)..(4)  
 ; OTHER INFORMATION:  
 ; FEATURE:  
 ; NAME/KEY: mat peptide  
 ; LOCATION: (65)..(1)  
 ; OTHER INFORMATION: Product= Sodium-channel modifier toxin  
 ; FEATURE:  
 ; NAME/KEY: sig peptide  
 ; LOCATION: (5)..(64)  
 ; OTHER INFORMATION:  
 ; US-10-721-793-113

Query Match 100.0%; Score 192; DB 9; Length 323;  
 Best Local Similarity 100.0%; Pred. No. 1.3e-53;  
 Matches 192; Conservative 0; Mismatches 0; Indels 0; Gaps 0;  
 QY 1 AAGACGGTTATCTGGTGACAGACGGCTGCAATACACTTGTGGATATTGGGAA 60  
 DB 65 AAGACGGTTATCTGGTGACAGACGGCTGCAATACACTTGTGGATATTGGGAA 124  
 QY 61 AACAAATCTGCAATAGGGAATGCATCGAAGCACCAGGAGGTAAATACGGCTATTGC 120  
 DB 125 AACAAATCTGCAATAGGGAATGCATCGAAGCACCAGGAGGTAAATACGGCTATTGC 184  
 QY 121 TAGCGATTGGGTCTATTGCGAAGGATTGTCCGATAGTACACCGACTTGGCCCTTTCT 180  
 DB 185 TAGCGATTGGGTCTATTGCGAAGGATTGTCCGATAGTACACCGACTTGGCCCTTTCT 244  
 QY 181 AATAAAGATGC 192  
 DB 245 AATAAAGATGC 256

## RESULT 3

US-10-721-793-119  
 ; Sequence 119, Application US/10721793  
 ; Publication No. US20050065331A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Corona Villegas, Miguel  
 ; APPLICANT: Garcia Rodriguez, Ma Consuelo  
 ; APPLICANT: Valdez Cruz, Norma Adriana  
 ; APPLICANT: Gurrola Briones, Georgina  
 ; APPLICANT: Becerril Lujan, Baltazar  
 ; APPLICANT: Possani Postay, Lourival Domingos  
 ; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the  
 ; FILE REFERENCE: 2099.0070001  
 ; CURRENT APPLICATION NUMBER: US/10/721,793  
 ; CURRENT FILING DATE: 2003-11-26  
 ; PRIOR APPLICATION NUMBER: US 60/430,067  
 ; PRIOR FILING DATE: 2002-12-02  
 ; NUMBER OF SEQ ID NOS: 294  
 ; SOFTWARE: Patent in version 3.1  
 ; SEQ ID NO 119  
 ; LENGTH: 192  
 ; TYPE: DNA  
 ; ORGANISM: Centruroides elegans  
 ; FEATURE:  
 ; NAME/KEY: CDS  
 ; LOCATION: (1)..(192)  
 ; OTHER INFORMATION: Product= Sodium-channel modifier toxin  
 ; US-10-721-793-119

Query Match 99.2%; Score 190.4; DB 9; Length 192;  
 Best Local Similarity 99.5%; Pred. No. 3.6e-53;  
 Matches 191; Conservative 0; Mismatches 1; Indels 0; Gaps 0;  
 QY 1 AAGACGGTTATCTGGTGACAGACGGCTGCAATACACTTGTGGATATTGGGAA 60  
 DB 1 AAGACGGTTATCTGGTGACAGACGGCTGCAATACACTTGTGGATATTGGGAA 60  
 QY 61 AACAAATCTGCAATAGGGAATGCATCGAAGCACCAGGAGGTAAATACGGCTATTGC 120  
 DB 61 AACAAATCTGCAATAGGGAATGCATCGAAGCACCAGGAGGTAAATACGGCTATTGC 120  
 QY 121 TAGCGATTGGGTCTATTGCGAAGGATTGTCCGATAGTACACCGACTTGGCCCTTTCT 180  
 DB 121 TAGCGATTGGGTCTATTGCGAAGGATTGTCCGATAGTACACCGACTTGGCCCTTTCT 180  
 QY 181 AATAAAGATGC 192  
 DB 181 AATAAAGATGC 192

## RESULT 4

US-10-721-793-117  
 ; Sequence 117, Application US/10721793  
 ; Publication No. US20050065331A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Corona Villegas, Miguel  
 ; APPLICANT: Garcia Rodriguez, Ma Consuelo  
 ; APPLICANT: Valdez Cruz, Norma Adriana  
 ; APPLICANT: Gurrola Briones, Georgina  
 ; APPLICANT: Becerril Lujan, Baltazar  
 ; APPLICANT: Possani Postay, Lourival Domingos  
 ; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the  
 ; FILE REFERENCE: 2099.0070001  
 ; CURRENT APPLICATION NUMBER: US/10/721,793  
 ; CURRENT FILING DATE: 2003-11-26  
 ; PRIOR APPLICATION NUMBER: US 60/430,067  
 ; PRIOR FILING DATE: 2002-12-02  
 ; NUMBER OF SEQ ID NOS: 294  
 ; SOFTWARE: Patent in version 3.1  
 ; SEQ ID NO 117

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; LENGTH: 323
; TYPE: DNA
; ORGANISM: Centrurioles elegans
; FEATURE:
; NAME/KEY: CDS
; LOCATION: (5)..(265)
; OTHER INFORMATION: Product= Sodium-channel modifier toxin precursor
; OTHER INFORMATION: In the mature peptide, the last Cys is amidated, and the last Gly
; OTHER INFORMATION: and the last 2 basic aminoacids are cut
; FEATURE:
; NAME/KEY: 3'UTR
; LOCATION: (269)..(323)
; OTHER INFORMATION:
; FEATURE:
; NAME/KEY: 5'UTR
; LOCATION: (1)..(4)
; OTHER INFORMATION:
; FEATURE:
; NAME/KEY: mat_peptide
; LOCATION: (65)..(1)
; OTHER INFORMATION: Product= Sodium-channel modifier toxin
; FEATURE:
; NAME/KEY: sig_peptide
; LOCATION: (5)..(64)
; OTHER INFORMATION:

```

US-10-721-793-117

```

Query Match      99.2%; Score 190.4; DB 9; Length 323;
Best Local Similarity 99.5%; Pred. No. 4.5e-53;
Matches 191; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

QY 1 AAAGCGGTTATCTGCTGGACAGACGGGCTGCAAAATACACTTGTCTGATATTGGAGAA 60
DB 65 AAAGCGGTTATCTGCTGGACAGACGGGCTGCAAAATACACTTGTCTGATATTGGAGAA 124
QY 61 AACAAATCTGCAATAGGAGATGCACATGGAAGCCGAGGAGGTAAATTACGGCTATTGC 120
DB 125 AACAAATCTGCAATAGGAGATGCACATGGAAGCCGAGGAGGTAAATTACGGCTATTGC 184
QY 121 TACCGATTGGGTGCTATTGCGAAGGATTTCCGATAGTACACCACTTGGCCCTTTCT 180
DB 185 TACCGATTGGGTGCTATTGCGAAGGATTTCCGATAGTACACCACTTGGCCCTTTCT 244
QY 181 AATAAAGATGC 192
DB 245 AATAAAGATGC 256

```

```

RESULT 5
US-10-721-793-151
; Sequence 151, Application US/10721793
; Publication No. US2005006531A1
; GENERAL INFORMATION:
; APPLICANT: Corona Villegas, Miguel
; APPLICANT: Garcia Rodriguez, Ma Consuelo
; APPLICANT: Valdez Cruz, Norma Adriana
; APPLICANT: Gurrea Briones, Georgina
; APPLICANT: Becerril Lujan, Baltazar
; APPLICANT: Posasani Postay, Lourival Domingos
; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the
; TITLE OF INVENTION: Venom of Scorpions of the Genus Centrurioles
; FILE REFERENCE: 2099.0070001
; CURRENT APPLICATION NUMBER: US/10721,793
; PRIOR FILING DATE: 2003-11-26
; PRIOR APPLICATION NUMBER: US 60/430,067
; NUMBER OF SEQ ID NOS: 294
; SOFTWARE: Patent in version 3.1
; SEQ ID NO 151
; LENGTH: 192
; TYPE: DNA
; ORGANISM: Centrurioles sculpturatus
; FEATURE:

```

```

; NAME/KEY: CDS
; LOCATION: (1)..(192)
; OTHER INFORMATION: Product= Sodium-channel modifier toxin
; PUBLICATION INFORMATION:
; AUTHORS: Corona, M., Valdez-Cruz, N.A., Merino, E., Zurita, M. & Posasani L.D.
; TITLE: Genes and peptides from the scorpion Centrurioles sculpturatus Ewing.
; JOURNAL: Toxicon
; VOLUME: 39
; ISSUE: 12
; PAGES: 1893-1898
; DATE: 2001-12-01
; DATABASE ENTRY DATE:
; RELEVANT RESIDUES: (1)..(192)
US-10-721-793-151

Query Match      81.7%; Score 156.8; DB 9; Length 192;
Best Local Similarity 88.5%; Pred. No. 6.1e-42;
Matches 170; Conservative 0; Mismatches 22; Indels 0; Gaps 0;

QY 1 AAAGCGGTTATCTGCTGGACAGACGGGCTGCAAAATACACTTGTCTGATATTGGAGAA 60
DB 1 AAAGCGGTTATCTGCTGGACAGACGGGCTGCAAAATACACTTGTCTGATATTGGAGAA 60
QY 61 AACAAATCTGCAATAGGAGATGCACATGGAAGCCGAGGAGGTAAATTACGGCTATTGC 120
DB 61 AACAAATCTGCAATAGGAGATGCACATGGAAGCCGAGGAGGTAAATTACGGCTATTGC 120
QY 121 TACCGATTGGGTGCTATTGCGAAGGATTTCCGATAGTACACCACTTGGCCCTTTCT 180
DB 121 TACCGATTGGGTGCTATTGCGAAGGATTTCCGATAGTACACCACTTGGCCCTTTCT 180
QY 181 AATAAAGATGC 192
DB 181 AATAAAGATGC 192

```

RESULT 6

```

US-10-721-793-149
; Sequence 149, Application US/10721793
; Publication No. US2005006531A1
; GENERAL INFORMATION:
; APPLICANT: Corona Villegas, Miguel
; APPLICANT: Garcia Rodriguez, Ma Consuelo
; APPLICANT: Valdez Cruz, Norma Adriana
; APPLICANT: Gurrea Briones, Georgina
; APPLICANT: Becerril Lujan, Baltazar
; APPLICANT: Posasani Postay, Lourival Domingos
; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the
; TITLE OF INVENTION: Venom of Scorpions of the Genus Centrurioles
; FILE REFERENCE: 2099.0070001
; CURRENT APPLICATION NUMBER: US/10721,793
; CURRENT FILING DATE: 2003-11-26
; PRIOR APPLICATION NUMBER: US 60/430,067
; PRIOR FILING DATE: 2002-12-02
; NUMBER OF SEQ ID NOS: 294
; SOFTWARE: Patent in version 3.1
; SEQ ID NO 149
; LENGTH: 320
; TYPE: DNA
; ORGANISM: Centrurioles sculpturatus
; FEATURE:
; NAME/KEY: CDS
; LOCATION: (5)..(262)
; OTHER INFORMATION: Product= Sodium-channel modifier toxin precursor
; OTHER INFORMATION: In the mature peptide, the last Cys is amidated, and the last Gl
; OTHER INFORMATION: and the last 2 basic aminoacids are cut
; FEATURE:
; NAME/KEY: mat_peptide
; LOCATION: (62)..(1)
; OTHER INFORMATION: Product= Sodium-channel modifier toxin
; FEATURE:
; NAME/KEY: sig_peptide

```

```

/ LOCATION: (5)..(61)
/ OTHER INFORMATION:
/ FEATURE:
/ NAME/KEY: 3'UTR
/ LOCATION: (266)..(320)
/ OTHER INFORMATION:
/ FEATURE:
/ NAME/KEY: 5'UTR
/ LOCATION: (1)..(4)
/ OTHER INFORMATION:
/ PUBLICATION INFORMATION:
/ AUTHORS: Corona, M., Valdez-Cruz, N.A., Merino, E., Zurita, M. & Possani L.D.
/ TITLE: Genes and peptides from the scorpion Centruroides sculpturatus Ewing,
/ TITLE: that recognize Na+-channels
/ JOURNAL: Toxicon
/ VOLUME: 39
/ ISSUE: 12
/ PAGES: 1893-1898
/ DATE: 2001-12-01
/ DATABASE ENTRY DATE:
/ RELEVANT RESIDUES: (5)..(262)
US-10-721-793-149

Query Match      81.7%; Score 156.8; DB 9; Length 320;
Best Local Similarity 88.5%; Pred. No. 7.6e-42;
Matches 170; Conservative 0; Mismatches 22; Indels 0; Gaps 0;

QY 1 AAGACGGTTATCTGCTGGACAGACGGCTGCAATACATCTCTGGATATTGGAGAA 60
DB 62 AAGACGGTTATCTGCTGGACAGACGGCTGCAATACATCTCTGGATATTGGAGAA 121
QY 61 AACAAATCTGCAATAGGGAATGCACATGGAAGCACCGAGGAGGTAAATTACGGCTATTGC 120
DB 122 AAGCATTTTGGCAATAGGGAATGCACATGGAAGCACCATAGGAGGTATTGCTATTTC 181
QY 121 TAGCGATTGGGTGCTATTGCGAAGGATTTGCGATAGTACACCGACTTGGCCCTTTCT 180
DB 182 TAGCGATTGGGTGCTATTGCGAAGGATTTGCGATAGTACACCGACTTGGCCCTTTCT 241
QY 181 AATAAAGATGC 192
DB 242 AATAAAGATGC 253

RESULT 7
US-10-721-793-195
/ Sequence 195, Application US/10721793
/ Publication No. US20050065331A1
/ GENERAL INFORMATION:
/ APPLICANT: Corona Villegas, Miguel
/ APPLICANT: Garcia Rodriguez, Ma Consuelo
/ APPLICANT: Valdez Cruz, Norma Adriana
/ APPLICANT: Gurtola Briones, Georgina
/ APPLICANT: Becerril Lujan, Baltazar
/ APPLICANT: Possani Postay, Lourival Domingos
/ TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the
/ TITLE REFERENCE: 2099.0070001
/ CURRENT APPLICATION NUMBER: US/10/721,793
/ CURRENT FILING DATE: 2003-11-26
/ PRIOR APPLICATION NUMBER: US 60/430,067
/ PRIOR FILING DATE: 2002-12-02
/ NUMBER OF SEQ ID NOS: 294
/ SOFTWARE: PatentIn version 3.1
/ SEQ ID NO 195
/ LENGTH: 192
/ TYPE: DNA
/ ORGANISM: Centruroides sculpturatus
/ FEATURE:
/ NAME/KEY: CDS
/ LOCATION: (5)..(262)
/ OTHER INFORMATION: Product= Sodium-channel modifier toxin precursor
/ OTHER INFORMATION: In the mature peptide, the last Cys is amidated, and the last Gly
/ OTHER INFORMATION: and the last 2 basic aminoacids are cut
/ FEATURE:
/ NAME/KEY: 5'clip
/ LOCATION: (266)..(320)
/ OTHER INFORMATION:
/ FEATURE:
/ NAME/KEY: 5'UTR
/ LOCATION: (1)..(4)
/ OTHER INFORMATION:
/ FEATURE:
/ NAME/KEY: mat_peptide

```

```

/ AUTHORS: Corona, M., Valdez-Cruz, N.A., Merino, E., Zurita, M. & Possani L.D.
/ TITLE: Genes and peptides from the scorpion Centruroides sculpturatus Ewing,
/ TITLE: that recognize Na+-channels
/ JOURNAL: Toxicon
/ VOLUME: 39
/ ISSUE: 12
/ PAGES: 1893-1898
/ DATE: 2001-12-01
/ DATABASE ENTRY DATE:
/ RELEVANT RESIDUES: (1)..(192)
US-10-721-793-195

Query Match      80.8%; Score 155.2; DB 9; Length 192;
Best Local Similarity 88.0%; Pred. No. 2.1e-41;
Matches 169; Conservative 0; Mismatches 23; Indels 0; Gaps 0;

QY 1 AAGACGGTTATCTGCTGGACAGACGGCTGCAATACATCTCTGGATATTGGAGAA 60
DB 1 AAGGAAGGTTATCTGCTGGACAGCTAAAGGGCTGCAAAAAAATTCCTGGAATTTGGAGAT 60
QY 61 AACAAATCTGCAATAGGGAATGCACATGGAAGCACCGAGGAGGTAAATTACGGCTATTGC 120
DB 61 AAGCATTTTGGCAATAGGGAATGCACATGGAAGCACATAGGAGGTAGTTACGGCTATTGC 120
QY 121 TAGCGATTGGGTGCTATTGCGAAGGATTTGCGATAGTACACCGACTTGGCCCTTTCT 180
DB 121 TAGCGATTGGGTGCTATTGCGAAGGATTTGCGATAGTACACCGACTTGGCCCTTTCT 180
QY 181 AATAAAGATGC 192
DB 181 AATAAAGATGC 192

RESULT 8
US-10-721-793-193
/ Sequence 193, Application US/10721793
/ Publication No. US20050065331A1
/ GENERAL INFORMATION:
/ APPLICANT: Corona Villegas, Miguel
/ APPLICANT: Garcia Rodriguez, Ma Consuelo
/ APPLICANT: Valdez Cruz, Norma Adriana
/ APPLICANT: Gurtola Briones, Georgina
/ APPLICANT: Becerril Lujan, Baltazar
/ APPLICANT: Possani Postay, Lourival Domingos
/ TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the
/ TITLE REFERENCE: 2099.0070001
/ CURRENT APPLICATION NUMBER: US/10/721,793
/ CURRENT FILING DATE: 2003-11-26
/ PRIOR APPLICATION NUMBER: US 60/430,067
/ PRIOR FILING DATE: 2002-12-02
/ NUMBER OF SEQ ID NOS: 294
/ SOFTWARE: PatentIn version 3.1
/ SEQ ID NO 193
/ LENGTH: 320
/ TYPE: DNA
/ ORGANISM: Centruroides sculpturatus
/ FEATURE:
/ NAME/KEY: CDS
/ LOCATION: (5)..(262)
/ OTHER INFORMATION: Product= Sodium-channel modifier toxin precursor
/ OTHER INFORMATION: In the mature peptide, the last Cys is amidated, and the last Gly
/ OTHER INFORMATION: and the last 2 basic aminoacids are cut
/ FEATURE:
/ NAME/KEY: 5'clip
/ LOCATION: (266)..(320)
/ OTHER INFORMATION:
/ FEATURE:
/ NAME/KEY: 5'UTR
/ LOCATION: (1)..(4)
/ OTHER INFORMATION:
/ FEATURE:
/ NAME/KEY: mat_peptide

```





Db 1 AAGGAGGTTATCTGGTGAAACAAAGACAGGCTGTAAATACAACACTGCTGATATTGGGA 60  
 Qy 58 GAAACAAATACCTGCAATAGGAGATGCACATGGAAGCAGCCGAGGAGTAATTACGGCTAT 117  
 Db 61 GAAACAAATACCTGCAATAGGAGATGCACATGGAAGCAGCCGAGGAGTAATTACGGCTAT 120  
 Qy 118 TGCTACGGATTGGGTGCTATTGTCGAAGGATTTGTCGATAGTACACCGACTTGGCCCTT 177  
 Db 121 TGCTACGGATTGGGTGCTATTGTCGAAGGATTTGTCGATAGTACACCGACTTGGCCCTT 180  
 Qy 178 TCTAATAAAGATGC 192  
 Db 181 CCTAATAAACATGC 195

## RESULT 14

US-10-721-793-89  
 ; Sequence 89, Application US/10721793  
 ; Publication No. US2005006531A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Corona Villegas, Miguel  
 ; APPLICANT: Garcia Rodriguez, Ma Consuelo  
 ; APPLICANT: Valdez Cruz, Norma Adriana  
 ; APPLICANT: Guriola Briones, Georgina  
 ; APPLICANT: Becerril Lujan, Baltazar  
 ; APPLICANT: Posasni Postay, Lourival Domingos  
 ; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the  
 ; TITLE OF INVENTION: Venom of Scorpions of the Genus Centruroides  
 ; FILE REFERENCE: 2099.0070001  
 ; CURRENT APPLICATION NUMBER: US/10/721,793  
 ; PRIOR FILING DATE: 2003-11-26  
 ; PRIOR APPLICATION NUMBER: US 60/430,067  
 ; PRIOR FILING DATE: 2002-12-02  
 ; NUMBER OF SEQ ID NOS: 294  
 ; SOFTWARE: Patent in version 3.1  
 ; SEQ ID NO 89  
 ; LENGTH: 323  
 ; TYPE: DNA  
 ; ORGANISM: Centruroides noxius  
 ; FEATURE:  
 ; NAME/KEY: CDS  
 ; LOCATION: (5)..(265)  
 ; OTHER INFORMATION: Product= Sodium-channel modifier toxin precursor  
 ; OTHER INFORMATION: In the mature peptide, the last Ser is amidated, and the last Gly  
 ; OTHER INFORMATION: and the last basic aminoacid are cut  
 ; PRIMER:  
 ; NAME/KEY: 3'UTR  
 ; LOCATION: (269)..(323)  
 ; OTHER INFORMATION:  
 ; FEATURE:  
 ; NAME/KEY: 5'UTR  
 ; LOCATION: (1)..(4)  
 ; OTHER INFORMATION:  
 ; FEATURE:  
 ; NAME/KEY: mat\_peptide  
 ; LOCATION: (62)..( )  
 ; OTHER INFORMATION: Product= Sodium-channel modifier toxin  
 ; FEATURE:  
 ; NAME/KEY: sig\_peptide  
 ; LOCATION: (5)..(61)  
 ; OTHER INFORMATION:  
 ; US-10-721-793-89

Query Match 75.7%; Score 145.4; DB 9; Length 323;  
 Best Local Similarity 87.7%; Pred. No. 4.9e-38;  
 Matches 171; Conservative 0; Mismatches 21; Indels 3; Gaps 1;

Qy 1 AAGGAGGTTATCTGGTGAAACAAAGACAGGCTGTAAATACAACACTGCTGATATTGGGA 57  
 Db 62 AAGGAGGTTATCTGGTGAAACAAAGACAGGCTGTAAATACAACACTGCTGATATTGGGA 121  
 Qy 58 GAAACAAATACCTGCAATAGGAGATGCACATGGAAGCAGCCGAGGAGTAATTACGGCTAT 117

Db 122 GAAACAAATACCTGCAATAGGAGATGCACATGGAAGCAGCCGAGGAGTAATTACGGCTAT 181  
 Qy 118 TGCTACGGATTGGGTGCTATTGTCGAAGGATTTGTCGATAGTACACCGACTTGGCCCTT 177  
 Db 182 TGCTACGGATTGGGTGCTATTGTCGAAGGATTTGTCGATAGTACACCGACTTGGCCCTT 241  
 Qy 178 TCTAATAAAGATGC 192  
 Db 242 CCTAATAAACATGC 256

## RESULT 15

US-10-721-793-111  
 ; Sequence 111, Application US/10721793  
 ; Publication No. US2005006531A1  
 ; GENERAL INFORMATION:  
 ; APPLICANT: Corona Villegas, Miguel  
 ; APPLICANT: Garcia Rodriguez, Ma Consuelo  
 ; APPLICANT: Valdez Cruz, Norma Adriana  
 ; APPLICANT: Guriola Briones, Georgina  
 ; APPLICANT: Becerril Lujan, Baltazar  
 ; APPLICANT: Posasni Postay, Lourival Domingos  
 ; TITLE OF INVENTION: Recombinant Immunogens for the Generation of Antivenoms to the  
 ; TITLE OF INVENTION: Venom of Scorpions of the Genus Centruroides  
 ; FILE REFERENCE: 2099.0070001  
 ; CURRENT APPLICATION NUMBER: US/10/721,793  
 ; PRIOR FILING DATE: 2003-11-26  
 ; PRIOR APPLICATION NUMBER: US 60/430,067  
 ; PRIOR FILING DATE: 2002-12-02  
 ; NUMBER OF SEQ ID NOS: 294  
 ; SOFTWARE: Patent in version 3.1  
 ; SEQ ID NO 111  
 ; LENGTH: 189  
 ; TYPE: DNA  
 ; ORGANISM: Centruroides elegans  
 ; FEATURE:  
 ; NAME/KEY: CDS  
 ; LOCATION: (1)..(189)  
 ; OTHER INFORMATION: Product= Sodium-channel modifier toxin  
 ; US-10-721-793-111

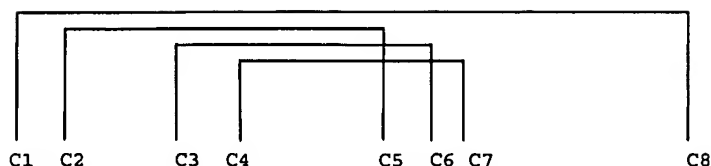
Query Match 66.0%; Score 126.8; DB 9; Length 189;  
 Best Local Similarity 82.8%; Pred. No. 6.4e-32;  
 Matches 159; Conservative 0; Mismatches 27; Indels 6; Gaps 1;

Qy 1 AAGGAGGTTATCTGGTGAAACAAAGACAGGCTGTAAATACAACACTGCTGATATTGGGA 60  
 Db 4 AAGGAGGTTATCTGGTGAAACAAAGACAGGCTGTAAATACAACACTGCTGATATTGGGA 63  
 Qy 61 AACAAATACCTGCAATAGGAGATGCACATGGAAGCAGCCGAGGAGTAATTACGGCTATTGC 120  
 Db 64 AACAAATACCTGCAATAGGAGATGCACATGGAAGCAGCCGAGGAGTAATTACGGCTATTGC 117  
 Qy 121 TACCGATTGGGTGCTATTGTCGAAGGATTTGTCGATAGTACACCGACTTGGCCCTTCT 180  
 Db 118 TATGCTTTTGGGTGCTATTGTCGAAGGATTTACCCGAAAGCGTACTGACCTGGCCCTTTCT 177  
 Qy 181 AATAAAGATGC 192  
 Db 178 GATTAACATGC 189

Search completed: January 22, 2006, 01:12:50  
 Job time : 2178 secs



Alignments:



# Long-chain toxins specific for sodium channels:

A	B	C	
004	Cex1	KEGYLVSKSTGCKYECFWLGKNEGCDKECKAPNQGGGYGYCHAFACWCENLPSTPTTYPIPGKSC	53.8
008	Cex2	KEGYLVSKSTGCKYECFWLGKNEGCDKECKAPNQGGGYGYCHAFACWCENLPSTPTTYPIPGKSC	53.8
036	Cex7	REGYLVSKSTGCKYECFWLGKNEGCDKECKAPNQGGGYGYCHAFACWCENLPSTPTTYPIPGKSC	52.3
028	Cex5	KDGYLVSKSTGCKYECFWLGKNEGCDKECKAPNQGGGYGYCHAFACWCENLPSTPTTYPIPGKSC	55.3
104	Ce6	KEGYLVNKSTGCKYSCVLLGKNENCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.0
108	Ce6b	KDGYLVNKSTGCKYSCVLLGKNENCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	63.0
148	CsEv3b	KEGYLVNKSTGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	63.0
176	CsEv2a	KEGYLVNKSTGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	62.1
164	CsEv2d	KEGYLVNKSTGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.6
160	CsEv2b	REGYLVNKSTGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.6
156	CsEv2c	KEGYLVNKSTGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.6
100	Ce5	KEGYLVNKSTGCKYGCCLLRKNEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	57.3
024	Cex4	KEGYLVNKSTGCKYECFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.0
032	Cex6	REGYLVNKSTGCKYECFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	58.4
020	Cex3	KDGYLVNKSTGCKYECFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	61.5
068	C115b	KEGYLVNKSTGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	62.1
072	C115c	KEGYLVNKSTGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	62.1
140	CsEvd	KDGYLVNKSTGCKYDCFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	63.0
144	CsEvlc	KDGYLVNKSTGCKYDCFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	63.0
168	CsEvlb	KEGYLVKKSDGCKYDCFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.0
172	CsEvlc	KEGYLVKKSDGCKYDCFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.0
084	C118	KEGYLVKKSDGCKYDCFWLGKNEFCDECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	60.0
092	Cn10b	KEGYLVNKSTGCKYCNCLILGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	74.2
124	Cg1	KDGYLVKKSDGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	52.3
128	Cg1b	KDGYLVKKSDGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	52.3
136	Cg3	KDGYLVKKSDGCKYGCCLKLGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	49.2
016	Cex13	KDGYLVIIKTGCKYCNCLILGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	66.1
112	Ce7	KDGYLVN-KTGCKYCNCLILGENEGCDKECKAKNQGGSYGYCYAFGCWCEGLPESTPTTYPIPGKSC	73.4
040	Cex8	KEGYLVNIYTGCKYSCWLLGENEYCIAC--KEIGAGYGYCHGFCWCEQFPENKPSYPPEKSC	55.3
052	Cex11	KEGYVPNIYTGCKYSCWLLGENEYCIAC--KEIGAGYGYCHGFCWCEQFPENKPSYPPEKSC	53.8
080	C117	KEGYLVNTYTGCKYICWKLGENKYCIDEC--KEIGAGYGYCHGFCWCEQFPENKPSYPPEKSC	67.6
044	Cex9	KDGYVPVE-VTGCKKSCYKLGENKFCNRECKMKHRGGSYGYCYFPGCYCEGLAESTPTWPLPNKSC	75.0
048	Cex10	KDGYLVE-VTGCKKSCYKLGENKFCNRECKMKHRGGSYGYCYFPGCYCEGLAESTPTWPLPNKSC	76.5
152	CsE1a	KDGYLVE-KTGCKKTCYKLGENDFCNRECKMKHIGGSYGYCYFPGCYCEGLAESTPTWPLPNKSC	79.6
196	CsE1x	KEGYLVD-VKGCKKNCKWKLGDNDYCLRECKKWKHIGGSYGYCYFPGCYCEGLAESTPTWPLPNKSC	76.5
116	Ce13	KDGYLVD-KTGCKYTCWILGENKYNRECKWKHRRGGSYGYCYFPGCYCEGLAESTPTWPLPNKSC	100.0
120	Ce13b	KDGYLVD-KTGCKYTCWILGENKYNRECKWKHRRGGSYGYCYFPGCYCEGLAESTPTWPLPNKSC	95.3
056	C112b	KEGYLVNHSTGCKYECYKLGNDNDYCLRECKQYQYKAGAGGYCYAFGCWCTHLYEQAVVWPLPKKTCN	51.5
088	Cn4b	KEGYLVNSYTGCKYECYKLGNDNDYCLRECKQYQYKAGAGGYCYAFGCWCTHLYEQAVVWPLPKKTCN	51.5
064	C114	KEGYLVNYHDGCKYECYKLGNDNDYCLRECKLRYGKAGAGGYCYAFGCWCTHLYEQAVVWPLPKKTCN	50.0
096	Ce3	KEGYLVNYHDGCKYECYKLGNDNDYCLRECKLRYGKAGAGGYCYAFGCWCTHLYEQAVVWPLPKKTCN	50.0
192	CsE3	KEGYLVNYHTGCKYECYKLGNDNDYCLRECKLRYGKAGAGGYCYAFGCWCTHLYEQAVVWPLPKKTCN	51.5
060	C113	KEGYLVNYHDGCKYECYKLGNDNDYCLRECKLRYGKAGAGGYCYAFGCWCTHLYEQAVVWPLPKKTCN	48.4
076	C116	KEGYLVNMKTGCKYGCYELGDNGYCDRCK--KAESGNYGYCYTVGCWCEGLPNKPTWPLPNKSC	62.1
188	CsE8	EKGYLVDHEDTGCRYKCTFSGENSYCDKECK--SQGDSGICQSKACYCQGLPEDTKTWPLIGKLC	49.2
132	Cg2	KDGYLVNKSTGCKYSCININDSHCNNECISSIRKGSYGYCYFPGCYCEGLAESTPTWPLPNKSC	50.0
180	CsE9b	EDGYLFDKRKRCTLECIDMTGDKNCDRCK--NEGGSFGKCSYFACWCKGLPGITPISRTPGKTCI	35.8
184	CsE9	EDGYLFDKRKRCTLECIDMTGDKNCDRCK--NEGGSFGKCSYFACWCKGLPGITPISRTPGKTCI	35.8
012	Cex12	NDGYLFDKRKRCTLECIDMTGDKNCDRCK--NEGGSFGKCSYFACWCKGLPGITPISRTPGKTCI	35.3

Column A= SEQ. ID. No.

Column B= Clone name

Column C= amino acid sequences encoded by the DNAs

Column D= Is the percent of identity to SEQ.ID.NO:116, the amino acid sequence (mature peptide) encoded by the elected sequence SEQ.ID.NO:115.